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NOV 17 2004
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client name: Metabasis Therapeutics, Inc.
date: November 17, 2004
client matter number: 45198.00014CON
pages (with cover): 27

to: U.S. Patent and
Trademark Office
company/office:
facsimile: (703) 872-9306
telephone:

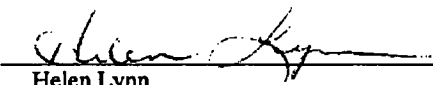
In re Application of:)
Qun Dang, et al.) Group Art Unit: 1624
Serial No.: 10/615,563) Examiner: Mark L. Berch
Filed: July 7, 2003) Customer No.: 36183
For: NOVEL PURINE INHIBITORS OF)
FRUCTOSE-1,6-)
BISPHOSPHATASE)

Attached hereto please find:

(1) Transmittal Form (PTO/SB/21) (1 pg.); Fee Transmittal (PTO/SB/17) (1 pg.);
Amendment and Remarks & Petition for Extension of Time (21 pgs.) and Terminal
Disclaimer (3 pgs.)

Certificate of Transmission under 37 CFR 1.8

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Helen Lynn

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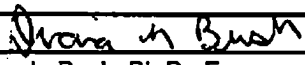
PTO/SB/21 (09-04)

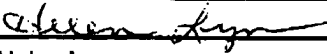
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| | | | |
|--|----------------------|------------------------|-----------------|
| TRANSMITTAL FORM <small>(to be used for all correspondence after initial filing)</small> | Application Number | 10/615,563 | |
| | Filing Date | July 7, 2003 | |
| | First Named Inventor | Qun Dang et al. | |
| | Art Unit | 1624 | |
| | Examiner Name | Mark L. Berch | |
| Total Number of Pages in This Submission | 27 | Attorney Docket Number | 45198.00014.CON |

| ENCLOSURES (Check all that apply) | | |
|---|--|--|
| <input checked="" type="checkbox"/> Fee Transmittal Form <input type="checkbox"/> Fee Attached <input checked="" type="checkbox"/> Amendment/Reply <input type="checkbox"/> After Final <input type="checkbox"/> Affidavits/declaration(s) <input checked="" type="checkbox"/> Extension of Time Request <input type="checkbox"/> Express Abandonment Request <input type="checkbox"/> Information Disclosure Statement <input type="checkbox"/> Certified Copy of Priority Document(s) <input type="checkbox"/> Response to Missing Parts/ Incomplete Application <input type="checkbox"/> Response to Missing Parts under 37 CFR 1.52 or 1.53 | <input type="checkbox"/> Drawing(s) <input type="checkbox"/> Licensing-related Papers <input type="checkbox"/> Petition <input type="checkbox"/> Petition to Convert to a Provisional Application <input type="checkbox"/> Power of Attorney, Revocation Change of Correspondence Address <input type="checkbox"/> Terminal Disclaimer <input type="checkbox"/> Request for Refund <input type="checkbox"/> CD, Number of CD(s) _____ <input type="checkbox"/> Landscape Table on CD | <input type="checkbox"/> After Allowance Communication to TC <input type="checkbox"/> Appeal Communication to Board of Appeals and Interferences <input type="checkbox"/> Appeal Communication to TC (Appeal Notice, Brief, Reply Brief) <input type="checkbox"/> Proprietary Information <input type="checkbox"/> Status Letter <input checked="" type="checkbox"/> Other Enclosure(s) (please identify below): Terminal Disclaimer (3 pgs.) |
| Remarks | | |

| SIGNATURE OF APPLICANT, ATTORNEY, OR AGENT | | | |
|--|---|----------|--------|
| Firm Name | PAUL, HASTINGS, JANOFSKY & WALKER LLP | | |
| Signature |  | | |
| Printed name | Diana L. Bush, Ph.D., Esq. | | |
| Date | November 17, 2004 | Reg. No. | 51,109 |

| CERTIFICATE OF TRANSMISSION/MAILING | | | |
|---|---|------|-------------------|
| I hereby certify that this correspondence is being facsimile transmitted to the USPTO or deposited with the United States Postal Service with sufficient postage as first class mail in an envelope addressed to: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450 on the date shown below. | | | |
| Signature |  | | |
| Typed or printed name | Helen Lynn | Date | November 17, 2004 |

This collection of information is required by 37 CFR 1.5. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.11 and 1.14. This collection is estimated to 2 hours to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

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PTO/SB/17 (10-04v2)

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FEE TRANSMITTAL
for FY 2005

Effective 10/01/2003. Patent fees are subject to annual revision.

☐ Applicant claims small entity status. See 37 CFR 1.27

TOTAL AMOUNT OF PAYMENT (\$1090)

Complete if Known

| | |
|----------------------|-----------------|
| Application Number | 10/615,563 |
| Filing Date | July 7, 2003 |
| First Named Inventor | Qun Dang et al. |
| Examiner Name | Mark L. Berch |
| Art Unit | 1624 |
| Attorney Docket No. | 45198.00014.CON |

METHOD OF PAYMENT (check all that apply)☐ Check ☐ Credit card ☐ Money ☐ Other ☐ None☒ Deposit Account

Deposit Account Number

50-2613

Deposit Account Name

The Director is authorized to: (check all that apply)

☒ Charge fee(s) indicated below ☐ Credit any overpayments☒ Charge any additional fee(s) or any underpayment of fee(s)☐ Charge fee(s) indicated below, except for the filing fee to the above-identified deposit account.**FEE CALCULATION****1. BASIC FILING FEE**

| Large Entity | | Small Entity | | Fee Description | Fee Paid |
|---------------------|----------|--------------|----------|------------------------|----------|
| Fee Code | Fee (\$) | Fee Code | Fee (\$) | | |
| 1001 | 790 | 2001 | 395 | Utility filing fee | |
| 1002 | 350 | 2002 | 175 | Design filing fee | |
| 1003 | 550 | 2003 | 275 | Plant filing fee | |
| 1004 | 790 | 2004 | 395 | Reissue filing fee | |
| 1005 | 180 | 2005 | 80 | Provisional filing fee | |
| SUBTOTAL (1) | | | | (\$) | 0 |

2. EXTRA CLAIM FEES FOR UTILITY AND REISSUE

| Total Claims | | Extra Claims | | Fee from below | Fee Paid |
|--------------|--------------------|--------------|-----|----------------|----------|
| Independent | Multiple Dependent | 20** | 3** | | |
| | | | | | 0 |
| | | | | | 0 |
| | | | | | 0 |

| Large Entity | | Small Entity | | Fee Description | Fee Paid |
|---------------------|----------|--------------|----------|--|----------|
| Fee Code | Fee (\$) | Fee Code | Fee (\$) | | |
| 1202 | 18 | 2202 | 9 | Claims in excess of 20 | |
| 1201 | 88 | 2201 | 44 | Independent claims in excess of 3 | |
| 1203 | 300 | 2203 | 150 | Multiple dependent claim, if not paid | |
| 1204 | 88 | 2204 | 44 | ** Reissue independent claims over original patent | |
| 1205 | 18 | 2205 | 9 | ** Reissue claims in excess of 20 over original patent | |
| SUBTOTAL (2) | | | | (\$) | 0 |

**or number previously paid, if greater. For Reissues, see above

FEE CALCULATION (continued)**3. ADDITIONAL FEES**

| Large Entity | | Small Entity | | Fee Description | Fee Paid |
|---|----------|--------------|----------|--|-------------|
| Fee Code | Fee (\$) | Fee Code | Fee (\$) | | |
| 1051 | 130 | 2051 | 65 | Surcharge - late filing fee or oath | |
| 1052 | 50 | 2052 | 25 | Surcharge - late provisional filing fee or cover sheet | |
| 1053 | 130 | 1053 | 130 | Non-English specification | |
| 1812 | 2,520 | 1812 | 2,520 | For filing a request for ex parte reexamination | |
| 1804 | 920* | 1804 | 920* | Requesting publication of SIR prior to Examiner action | |
| 1806 | 1,840* | 1806 | 1,840* | Requesting publication of SIR after Examiner action | |
| 1251 | 110 | 2251 | 55 | Extension for reply within first month | |
| 1252 | 430 | 2252 | 215 | Extension for reply within second month | |
| 1253 | 980 | 2253 | 490 | Extension for reply within third month | 980 |
| 1254 | 1,530 | 2254 | 765 | Extension for reply within fourth month | |
| 1255 | 2,080 | 2255 | 1,040 | Extension for reply within fifth month | |
| 1401 | 340 | 2401 | 170 | Notice of Appeal | |
| 1402 | 340 | 2402 | 170 | Filing a brief in support of an appeal | |
| 1403 | 300 | 2403 | 150 | Request for oral hearing | |
| 1451 | 1,510 | 1451 | 1,510 | Petition to institute a public use proceeding | |
| 1452 | 110 | 2452 | 55 | Petition to revive - unavoidable | |
| 1453 | 1,370 | 2453 | 685 | Petition to revive - unintentional | |
| 1501 | 1,370 | 2501 | 685 | Utility issue fee (or reissue) | |
| 1502 | 480 | 2502 | 245 | Design issue fee | |
| 1503 | 680 | 2503 | 330 | Plant issue fee | |
| 1460 | 130 | 1460 | 130 | Petitions to the Commissioner | |
| 1807 | 50 | 1807 | 50 | Processing fee under 37 CFR 1.17(q) | |
| 1808 | 180 | 1808 | 180 | Submission of Information Disclosure Stmt | |
| 8021 | 40 | 8021 | 40 | Recording each patent assignment per property (times number of properties) | |
| 1809 | 790 | 2809 | 395 | Filing a submission after final rejection (37 CFR 1.129(a)) | |
| 1810 | 790 | 2810 | 395 | For each additional invention to be examined (37 CFR 1.129(b)) | |
| 1801 | 790 | 2801 | 395 | Request for Continued Examination (RCE) | |
| 1802 | 900 | 1802 | 900 | Request for expedited examination of a design application | |
| Other fee (Specify) Code 1814/2814 Statutory Disclaimer Fee | | | | | 110 |
| * Reduced by Basic Filing Fee Paid | | | | SUBTOTAL (3) | 1090 |

SUBMITTED BY

| | | | | | |
|-------------------|----------------------------|-----------------------------------|-------------------|-----------|----------------|
| Name (Print/Type) | Diana L. Bush, Ph.D., Esq. | Registration No. (Attorney/Agent) | 51,109 | Telephone | (858) 720-2500 |
| Signature | <i>Diana L. Bush</i> | Date | November 17, 2004 | | |

(Complete if applicable)

WARNING: Information on this form may become public. Credit card information should not be included on this form. Provide credit card information and authorization on PTO-2038.

This collection of information is required by 37 CFR 1.17 and 1.27. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 12 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

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Patent
45198.00014.CON1

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

| | | | |
|-------------|-------------------------|---|-------------------------|
| Applicants: | Qun Dang <i>et al.</i> |) | |
| | |) | Group Art Unit: 1624 |
| Serial No.: | 10/615,563 |) | |
| | |) | Examiner: Mark L. Berch |
| Filed: | July 7, 2003 |) | |
| | |) | Customer No.: 36183 |
| Title: | NOVEL PURINE INHIBITORS |) | |
| | OF FRUCTOSE-1,6- |) | |
| | BISPHOSPHATASE |) | |
| | |) | |
| | |) | |

TERMINAL DISCLAIMER UNDER 37 C.F.R. §1.321(b)

Mail Stop Amendment
Commissioner for Patents
P. O. Box 1450
Alexandria, VA 22313-1450

Dear Sir:

Metabasis Therapeutics, Inc., a corporation duly organized under the laws of the State of Delaware, having a principal office located at 9390 Towne Centre Drive, San Diego, California 92121, and duly represented by the undersigned, represents that it is the assignee of the full title

CERTIFICATE OF TRANSMISSION
(37 C.F.R. §1.8)

I hereby certify that this paper (along with anything referred to as being attached or enclosed) is being facsimile transmitted to the United States Patent and Trademark Office on the date shown below.

November 17, 2004
Date of Transmission
SAN/102479.1 45198.00014

Helen Lynn
Name of Person Transmitting Paper


Signature of Person Transmitting Paper

Patent
45198.00014.CON1

and interest in and to the above-identified Application Serial No. 10/615,563, filed July 7, 2003, as evidenced by the deed of Assignment recorded on June 4, 1998 at Reel 009224, Frame 0348.

Metabasis Therapeutics, Inc., hereby disclaims, except as provided below, the terminal part of the statutory term of any patent granted on Application Serial 10/615,563 which would extend beyond the expiration date of the full statutory term of prior U.S. Patent No. 6,284,748, the term being defined in 35 U.S.C. 154 to 156. Metabasis Therapeutics, Inc. hereby agrees that any patent granted on Application Serial No. 10/615,563 shall be enforceable only for and during such period that such patent and prior U.S. Patent No. 6,284,748, are commonly owned. This agreement runs with any patent granted on the instant application and is binding upon the grantee, its successors or assigns.

In making the above disclaimer, Metabasis Therapeutics, Inc. does not disclaim the terminal part of any patent granted on the instant application that would extend to the expiration date of the full statutory term as defined in 35 U.S.C. 154 to 156 of U.S. Patent No. 6,284,748, as presently shortened by any terminal disclaimer filed, in the event that it later: expires for failure to pay a maintenance fee, is held unenforceable, is found invalid by a court of competent jurisdiction, is statutorily disclaimed in whole or terminally disclaimed under 37 CFR 1.321, has all claims canceled by a reexamination certificate, is reissued, or is in any manner terminated prior to the expiration of its full statutory term as presently shortened by any terminal disclaimer.

I hereby declare that all statements made herein of my own knowledge are true, and that all statements made on information and belief are believed to be true; and further, that these statements are made with the knowledge that willful false statements, and the like so made, are punishable by fine or imprisonment, or both, under Section 1001, Title 18 of the United States

Code, and that such willful false statements may jeopardize the validity of the application or any patent issuing thereon.

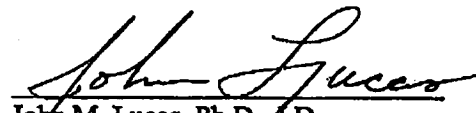
The undersigned is an attorney of record.

Patent
45198.00014.CON1

The Commissioner is hereby authorized to charge Deposit Account No. 50-2613 for the fee due herein and any other fees that may become due or credit become payable during the pendency of this application.

Respectfully submitted,

Dated: Nov 17, 2004 By:


John M. Lucas, Ph.D., J.D.
Reg. No. 43,373

METABASIS THERAPEUTICS, INC.
9390 Towne Centre Drive, Bldg. 300
San Diego, CA 92121